REMARKS

Claims 45, 46, 49-60, 64-77, 79, 80, and 82-87 are pending. The claims have been amended to correct minor typographical errors and to more clearly indicate what applicants regard as the subject matter of the invention.

In accordance with 37 C.F.R. §1.121, applicants have provided (1) accurate instructions to amend the claims, (2) replacement claims in clean form herein, and (3) another version of the amended claims marked up to show all the changes relative to the previous version of the claims, which appears on an attached page.

I. Double Patenting Rejection

Claims 76, 77, 79, 80 and 82-87 have been rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over Claims 1-6 of U.S. Patent No. 6,284,741. In response, to ensure an allowance of the present application, Applicants file herewith a Terminal Disclaimer.

II. Rejections under 35 U.S.C. § 112

Claims 45, 46, 49-60, 64-77, 79, 80 and 82-87 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Specifically, the Examiner has alleged that the claims are indefinite due to the recitation of the phrase "chemical analogue". The Examiner states that one of skill in the art would not know what compounds are encompassed by the phrase "chemical analogue" because the metes and bounds of the phrase are unclear. The Examiner has alleged that the recitation "chemical analogue" in Claims 45-60 and 64-87 is indefinite.

Applicants submit that the term is clear and definite to one of ordinary skill in the art. The specification defines the term "chemical analogue" at page 25, lines 13-24, as a nucleic acid molecule having a modified base, nucleotide, nucleoside, or phosphate backbone. It is clear

from the referenced passage that the term does not extend to a change in the number or nucleotide sequence of bases. However, in the interest of securing an early allowance, Applicants have amended the claims such that the claims are directed to modified nucleic acid molecules, rather than chemical analogues, wherein the modification is a chemical modification that does not change the length or nucleotide sequence of the nucleic acid molecule. Applicants assert that the amendment to the claims makes clear that the compound is indeed a nucleic acid molecule and that the modified nucleic acid molecules have the same length and nucleotide sequence as the unmodified nucleic acid molecule, as long as the resultant modified nucleic acid molecule maintains the requisite activity of the unmodified nucleic acid molecule.

In view of the foregoing comments and amendments, withdrawal of the rejection of the claims under 35 U.S.C. § 112, second paragraph is respectfully requested.

III. Rejections under 35 U.S.C. § 102(b)

Claims 76 and 79 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,643,788 of Baserga et al., Delafontaine, and Low et al. (WO 98/22579) and under 35 U.S.C. § 102(e) as allegedly anticipated by Low et al. (U.S. Patent No. 6,071,891). Applicants respectfully traverse the rejections.

The Examiner has alleged that all of the cited art disclose 18-mers and 20-mers nucleic acid analogues of SEQ ID NO: 12. The 18-mers and 20-mers of the cited art are not within the scope of Claims 76 and 79, as presently amended, because the claims relate a modified nucleic acid molecule of SEQ ID NO:12, which is a 15mer, wherein the modification is a chemical modification of the nucleic acid that does not result in a change in length or nucleotide sequence of the nucleic acid molecule. Accordingly, withdrawal of the rejections under 35 U.S.C. §§ 102(b) and 102(e) is respectfully requested.

Claims 45-51, 54, 61-66, 69, 76, 78 and 81 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by WO 96/01636 to Werther et al. The Examiner alleges that Werther et al. disclose methods of treatment of skin disorders using an 18-mer DNA analogue of SEQ ID NO: 14. As discussed above, the claims include the nucleic acid molecule of SEQ ID NO: 14, and chemical modifications thereof, wherein the chemical modifications do not alter the length or nucleotide sequence of SEQ ID NO:14, which is a 15-mer. As such, the claims do not include the 18-mer nucleic acid molecule of Werther et al. Accordingly, since the cited references do not teach each and every limitation of the claims, withdrawal of the rejection under 35 U.S.C. § 102(b) is respectfully requested.

IV. Rejections Under 35 U.S.C. § 103(a)

Claims 45, 46, 50, 52, 64, 65 and 67 have been rejected under 35 U.S.C. § 103(a) as allegedly rendered obvious by U.S. Patent No. 5,929,040 to Werther et al. in view of U.S. Patent No. 6,071,891 to Low et al., WO 98/22579 to Low et al., WO 96/10401 to Delafontaine or U.S Patent No. 5,643,788 to Baserga. The Examiner has alleged that Werther et al. teach methods of treatment of skin disorders using antisense molecules that inhibit IGF-I, and that the secondary references teach chemical analogues of SEQ ID NO: 12 that are antisense inhibitors of IGF-I. Applicants respectfully submit that none of Werther et al. nor the secondary references teach the nucleic acid of SEQ ID NO: 12 or a chemical modification thereof, wherein the chemical modification does not change the length or nucleotide sequence of SEQ ID NO:12, as do the claims, as presently amended. Thus, the combination of cited references fails to achieve the present invention. Withdrawal of the rejection under 35 U.S.C. § 103(a) is thus respectfully requested.

V. Conclusion

In view of the foregoing comments and amendments, favorable consideration and allowance of all pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Applicants have submitted herewith the fee for a 3 month extension of time, up to and including May 1, 2003. Applicants believe that no additional fees are required in connection with this communication. However, if any additional fee is required in connection with this communication, the Commissioner is hereby authorized to charge such fee pursuant to 37 C.F.R. §1.17(p) to Deposit Account No. 02-4377. Two copies of this Response are enclosed.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Please amend Claims 45, 46, 49-60, 64-77, 79, 80, and 82-87 as follows.

45. (Twice Amended) A method for ameliorating the effects of a proliferative and/or inflammatory skin disorder in a mammal, said method comprising contacting the proliferating and/or inflamed skin with an effective amount of a nucleic acid molecule selected from the group consisting of 5'-ATCTCTCCGCTTCCTTTC-3' (SEQ ID NO:10); 5'-UCCGGAGCCAGACUU-3' (SEQ ID NO:12); 5'-CACAGUUGCUGCAAG-3' (SEQ ID NO:13); 5'-UCUCCGCUUCCUUUC-3' (SEQ ID NO:14); 5'-AGCCCCCACAGCGAG-3' (SEQ ID NO:15); 5'-GCCUUGGAGAUGAGC-3' (SEQ ID NO:16); 5'-UAACAGAGGUCAGCA-3' (SEQ ID NO:17); 5'-GGAUCAGGGACCAGU-3' (SEQ ID NO:18); 5'-CGGCAAGCUACACAG-5' (SEQ ID NO:19); 5'-GGCAGGCAGGCACAC-3' (SEQ ID NO:20) or chemical [analogue] modification of any one of said nucleic acid molecules, wherein said modification produces a modified nucleic acid molecule having a length and nucleotide sequence which is the same as the nucleic acid molecule prior to modification, and wherein the nucleic acid molecule [or its chemical analogue] or modified nucleic acid molecule is capable of reducing the level of IGF-I receptor in said mammal.

46. (Amended) [A] The method according to Claim 45 wherein the mammal is a human.

49. (Amended) [A] The method according to Claim 45 wherein the proliferative or inflammatory skin disorder is psoriasis, eczema, ichthyosis, pityriasis, rubra, pilaris, serborrhoea, keloids, keratosis, neoplasias, scleroderma, warts, benign growths or cancers of the skin.

50. (Amended) [A] The method according to Claim 49 wherein the skin condition is psoriasis.

51. (Amended) [A] The method according to Claim 45 herein the nucleic acid molecule is 5'-ATCTCTCCGCTTCCTTTC-3' (SEQ ID NO:10) or [chemical analogue] a modification thereof.

52. (Amended) [A] The method according to Claim 45 wherein the nucleic acid molecule is 5'-UCCGGAGCCAGACUU-3' (SEQ ID NO:12) or [chemical analogue] a modification thereof.

53. (Amended) [A] The method according to Claim 45 wherein the nucleic acid molecule is 5'-CACAGUUGCUGCAAG-3' (SEQ ID NO:13) or [chemical analogue] a modification thereof.

54. (Amended) [A] The method according to Claim 45 wherein the nucleic acid molecule is 5'-UCUCCGCUUCCUUUC-3' (SEQ ID NO:14) or [chemical analogue] a modification thereof.

55. (Amended) [A] The method according to Claim 45 wherein the nucleic acid molecule is 5'-AGCCCCCACAGCGAG-3' (SEQ ID NO:15) or [chemical analogue] a modification thereof.

56. (Amended) [A] The method according to Claim 45 herein the nucleic acid molecule is 5'-GCCUUGGAGAUGAGC-3' (SEQ ID NO:16) or [chemical analogue] a modification thereof.

57. (Amended) [A] The method according to Claim 45 wherein the nucleic acid molecule is 5'-UAACAGAGGUCAGCA-3' (SEQ ID NO:17) or [chemical analogue] a modification thereof.

58. (Amended) [A] The method according to Claim 45 wherein the nucleic acid molecule is 5'-GGAUCAGGGACCAGU-3' (SEQ ID NO:18) or [chemical analogue] a modification thereof.

59. (Amended) [A] The method according to Claim 45 wherein the nucleic acid molecule is 5'-CGGCAAGCUACACAG-5' (SEQ ID NO:19) or [chemical analogue] a modification thereof.

60. (Amended) [A] The method according to Claim 45 wherein the nucleic acid molecule is 5'-GGCAGGCAGGCACAC-3' (SEQ ID NO:20) or [chemical analogue] a modification thereof.

64. (Twice Amended) A method of ameliorating the effects of psoriasis in a mammal, said method comprising contacting proliferating skin with an effective amount of one or more nucleic acid molecules or [chemical analogues thereof] selected from the group consisting of 5'-ATCTCTCCGCTTCCTTTC-3' (SEQ ID NO:10); 5'-UCCGGAGCCAGACUU-3' (SEQ ID NO:12); 5'-CACAGUUGCUGCAAG-3' (SEQ ID NO:13); 5'-UCUCCGCUUCCUUUC-3' (SEQ ID NO:14); 5'-AGCCCCCACAGCGAG-3' (SEQ ID NO:15); 5'-GCCUUGGAGAUGAGC-3' (SEQ ID NO:16); 5'-UAACAGAGGUCAGCA-3' (SEQ ID NO:17); 5'-GGAUCAGGGACCAGU-3' (SEQ ID NO:18); 5'-CGGCAAGCUACACAG-5' (SEQ ID NO:19); 5'-GGCAGGCAGGCACAC-3' (SEQ ID NO:20) or chemical [analogue] modification of any one of said nucleic acid molecules, wherein said modification produces a modified nucleic acid molecule having a length and nucleotide sequence which is the same as the nucleic acid molecule prior to modification and wherein said nucleic acid molecule or modified nucleic acid molecule [which] is capable of interacting with mRNA transcribed from an IGF-I gene, an IGF-I receptor gene or a gene encoding an IGFBP.

65. (Amended) [A] The method according to Claim 64 wherein the mammal is a human.

66. (Amended) [A] The method according to Claim 64 herein the nucleic acid molecule is 5'-ATCTCTCCGCTTCCTTTC-3' (SEQ ID NO:10) or [chemical analogue] a modification thereof.

67. (Amended) [A] The method according to Claim 64 wherein the nucleic acid molecule is 5'-UCCGGAGCCAGACUU-3' (SEQ ID NO:12) or [chemical analogue] a modification thereof.

68. (Amended) [A] The method according to Claim 64 wherein the nucleic acid molecule is 5'-CACAGUUGCUGCAAG-3' (SEQ ID NO:13) or [chemical analogue] a modification thereof.

69. (Amended) [A] The method according to Claim 64 wherein the nucleic acid molecule is 5'-UCUCCGCUUCCUUUC-3' (SEQ ID NO:14) or [chemical analogue] a modification thereof.

70. (Amended) [A] The method according to Claim 64 wherein the nucleic acid molecule is 5'-AGCCCCCACAGCGAG-3' (SEQ ID NO:15) or [chemical analogue] a modification thereof.

71. (Amended) [A] The method according to Claim 64 wherein the nucleic acid molecule is 5'-GCCUUGGAGAUGAGC-3' (SEQ ID NO:16) or [chemical analogue] a modification thereof.

72. (Amended) [A] The method according to Claim 64 wherein the nucleic acid molecule is 5'-UAACAGAGGUCAGCA-3' (SEQ ID NO:17) or [chemical analogue] a modification thereof.

73. (Amended) [A] The method according to Claim 64 wherein the nucleic acid molecule is 5'-GGAUCAGGGACCAGU-3' (SEQ ID NO:18) or [chemical analogue] a modification thereof.

74. (Amended) [A] The method according to Claim 64 wherein the nucleic acid molecule is 5'-CGGCAAGCUACACAG-5' (SEQ ID NO:19) or [chemical analogue] a modification thereof.

75. (Amended) [A] The method according to Claim 64 wherein the nucleic acid molecule is 5'-GGCAGGCAGGCACAC-3' (SEQ ID NO:20) or [chemical analogue] a modification thereof.

76. (Twice Amended) A composition comprising a nucleic acid molecule selected from the group consisting of 5'-UCCGGAGCCAGACUU-3' (SEQ ID NO:12); 5'-CACAGUUGCUGCAAG-3' (SEQ ID NO:13); 5'-AGCCCCCACAGCGAG-3' (SEQ ID NO:15); 5'-GCCUUGGAGAUGAGC-3' (SEQ ID NO:16); 5'-UAACAGAGGUCAGCA-3' (SEQ ID NO:17); 5'-GGAUCAGGGACCAGU-3' (SEQ ID NO:18); 5'-CGGCAAGCUACACAG-5' (SEQ ID NO:19); 5'-GGCAGGCAGGCACAC-3' (SEQ ID NO:20) or chemical [analogue] modification of any one of said nucleic acid molecules, wherein said modification produces a modified nucleic acid molecule having a length and nucleotide sequence which is the same as the nucleic acid molecule prior to modification, and wherein said nucleic acid molecule or modified nucleic acid molecule [chemical analogue] is capable of reducing the level of IGF-I receptor in a mammal said composition further comprising one or more pharmaceutically acceptable carriers and/or diluents.

77. (Amended) [A] The composition according to Claim 76 wherein the mammal is a human.

79. (Amended) [A] The composition according to Claim 76 wherein the nucleic acid molecule is 5'-UCCGGAGCCAGACUU-3' (SEQ ID NO:12) or [chemical analogue] a modification thereof.

80. (Amended) [A] The composition according to Claim 76 wherein the nucleic acid molecule is 5'-CACAGUUGCUGCAAG-3' (SEQ ID NO:13) or [chemical analogue] a modification thereof.

82. (Amended) [A] The composition according to Claim 76 wherein the nucleic acid molecule is 5'-AGCCCCCACAGCGAG-3' (SEQ ID NO:15) or [chemical analogue] a modification thereof.

83. (Amended) [A] The composition according to Claim 76 wherein the nucleic acid molecule is 5'-GCCUUGGAGAUGAGC-3' (SEQ ID NO:16) or [chemical analogue] a modification thereof.

84. (Twice Amended) A composition according to Claim 76 wherein the nucleic acid molecule is 5'-UAACAGAGGUCAGCA-3' (SEQ ID NO:17) or [chemical analogue] a modification thereof.

85. (Amended) [A] The composition according to Claim 76 wherein the nucleic acid molecule is 5'-CGGCAAGCUACACAG-5' (SEQ ID NO:19) or [chemical analogue] a modification thereof.

86. (Amended) [A] The composition according to Claim 76 wherein the nucleic acid molecule is 5'-GGCAGGCAGGCACAC-3' (SEQ ID NO:20) or [chemical analogue] a modification thereof.

87. (Twice Amended) [A] The composition according to Claim 76 wherein the nucleic acid molecule is 5'-GGAUCAGGGACCAGU-3' (SEQ ID NO:18) or [chemical analogue] a modification thereof.